Haemophilus influenzae Infection (Invasive Disease)

Report Immediately

May-2003

1) THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Haemophilus influenzae is a pleomorphic gram-negative coccobacillus that may be either encapsulated (types a–f) or unencapsulated (nontypeable). Most cases of invasive diseases in children, before the introduction of *H. influenzae* type b (Hib) conjugate vaccination, were caused by type b. Type f is the most common other serotype causing invasive infections in United States.

B. Clinical Description and Laboratory Diagnosis

Invasive *H. influenzae* disease may produce various clinical syndromes, including meningitis, bacteremia or sepsis, epiglottitis, pneumonia, septic arthritis, osteomyelitis, pericarditis, empyema, periorbital and facial cellulitis, and abscesses. In contrast, mucosal infections such as bronchitis, sinusitis, and otitis, which can be caused by *H. influenzae* (usually not type b), are considered noninvasive disease.

Laboratory diagnosis is made by isolation of organisms from blood or CSF. Specific capsular polysaccharide may be identified by CIE or LA techniques.

C. Reservoir

Humans are the only known host.

D. Modes of Transmission

H. influenzae is transmitted person-to-person by droplet or direct contact with nasopharyngeal secretions of an infected person. The most common portal of entry is the nasopharynx. Inhaling amniotic fluid or genital tract secretions containing the organism can infect newborns.

E. Incubation Period

The incubation period is unknown but probably is 2–4 days.

F. Period of Communicability or Infectious Period

- **If not on antibiotic therapy**—as long as organisms are present in the upper respiratory tract, which may be for a prolonged period even without nasal discharge.
- **If on antibiotic therapy**—noncommunicable within 24–48 hours after starting effective antibiotic therapy.

The contagious potential of invasive *H. influenzae* disease is considered to be limited. However, certain circumstances, particularly close contact with a case (*e.g.,* in a household, daycare center, or institutional setting), can lead to outbreaks of Hib or direct secondary transmission of the disease. Asymptomatic colonization by *H. influenzae* strains is common; nonencapsulated strains are recovered from the throat of 60% to 90% of children. The exact period of communicability is unknown.

G. Epidemiology

H. influenzae invasive infection occurs worldwide and is most prevalent among children aged 2 months to 3 years. It is unusual in healthy individuals over the age of 5 years. In the United States, peak incidence is in children 6–12 months of age. Secondary cases may occur in households, daycare centers, and other institutional settings.

Before the widespread use of Hib conjugate vaccines, Hib was a leading cause of bacterial meningitis in the United States among children <5 years of age and a major cause of other life-threatening invasive bacterial diseases in this age group. Meningitis occurred in approximately two-thirds of children with invasive Hib disease, resulting in hearing impairment or severe permanent neurologic sequelae such as mental retardation, seizure, cognitive and developmental delay, and paralysis in 15–30% of survivors. Approximately 5% of all cases were fatal. Invasive Hib disease now is limited to unvaccinated or undervaccinated children and adults.

Invasive disease has been more frequent in boys, African Americans, Alaskan Eskimos, Apache and Navajo Indians, child care center attendees, children living in overcrowded conditions, and children who were not breastfed. Unimmunized children, particularly those younger than 4 years of age, who are in prolonged close contact (such as in a household setting) with a child with invasive Hib disease, are at an increased risk for invasive Hib disease. Other factors predisposing to invasive disease include sickle cell disease, asplenia, HIV infection, certain immunodeficiency syndromes, and malignant neoplasms. For 2001, 493 cases from the United States (33 from New Jersey) of invasive Hib disease among all ages were reported by the CDC. In New Jersey, an average of 50 cases of invasive disease among all ages were reported each year to the New Jersey Department of Health and Senior Services (NJDHSS).

2) REPORTING CRITERIA AND LABORATORY TESTING SERVICES

A. New Jersey Department of Health and Senior Services (NJDHSS) Case Definition

CASE CLASSIFICATION

A. CONFIRMED

A clinically compatible case, **AND**

- Isolation (culture) of *H. influenzae* from a normally sterile body site (blood, cerebrospinal fluid (CSF), or less commonly joint, pleural, or pericardial fluid).

B. PROBABLE

A clinically compatible case, **AND**

- Detection of Hib antigen in CSF.

Note: Positive antigen test results from urine or serum samples are unreliable, and therefore, not confirmatory.

C. POSSIBLE

Not used.

NOTE Isolates of *H. influenzae* must be submitted within the three (3) working days to the New Jersey Department of Health and Senior Services, Division of Public Health and Environmental Laboratories, Specimen Receiving and Records, P.O. Box 361, John Fitch Plaza, Trenton, NJ 08625-0361.

B. Laboratory Testing Services Available

Confirmation and serotyping of *H. influenzae* isolates are available at the NJDHSS Public Health and Environmental Laboratories (PHEL). All strains of *H. influenzae* isolated from normally sterile sites must be submitted within **three (3)** days to the PHEL (PHEL Specimen Receiving and Records, NJDHSS, CN 361 Trenton, NJ 08365) to identify the strain and to differentiate between serotype b and other serotypes. For more information on submitting specimens, contact the PHEL at 609.984.2514 or 609.292.7368.

Note: Positive antigen results from urine and/or serum samples are not reliable for diagnosis of *H. influenzae* disease and should not be used as a substitute for culture results.

3) DISEASE REPORTING AND CASE INVESTIGATION

A. Purpose of Surveillance and Reporting

- To ensure that all cases of invasive *H. influenzae* are typed and to identify all cases of Hib.
- To identify household and daycare contacts of Hib cases that need antimicrobial prophylaxis and/or immunization and to prevent further spread of the disease by Hib cases.
- To distinguish between failure to vaccinate and vaccine failure.

B. Laboratory and Healthcare Provider Reporting Requirements

The New Jersey Administrative Code (N.J.A.C. 8:57-1.8) stipulates that health care providers and laboratories **immediately report** (by telephone, confidential fax, over the Internet using Communicable Disease Reporting System (CDRS)) any suspect or known case of invasive *H. influenzae* to the local health officer having jurisdiction over the locality in which the patient lives, or, if unknown, to the health officer in whose jurisdiction the health care provider requesting the laboratory examination is located.
If this is not possible, call the Infectious and Zoonotic Diseases Program NJDHSS at 609.588.7500 during business hours, 609.392.2020 after business hours, on weekends and holidays. Such report shall be followed by a written or electronic report within 24 hours of the initial report

C. Local Department of Health Reporting and Follow-Up Responsibilities

1. **Reporting Requirements**

The New Jersey Administrative Code (N.J.A.C. 8:57-1.8) stipulates that each local health officer must **report immediately** the occurrence of any suspected or confirmed case of invasive *H. influenzae* disease, as defined by the reporting criteria in Section 2 A to NJDHSS, Infectious and Zoonotic Diseases at 609.588.7500 during business hours, 609.392.2020, after business hours, on weekends and holidays. A telephone report shall be followed up by a written or electronic report within 24 hours of the initial report or the report can be filed electronically over the Internet using the confidential and secure Communicable Disease Reporting System (CDRS).

2. **Case Investigation**

a. **The most important step a local health officer can take if he/she learns of any case of invasive *H. influenzae* disease is to call the NJDHSS immediately, any time of the day or night. Daytime phone number of the Infectious and Zoonotic Program NJDHSS is 609.588.7500. The emergency phone number for nights and weekends is 609.392.2020.**

b. After notification to the IZDP, it is the health officer's responsibility to complete a CDS-1 Reporting Form by interviewing the patient and/or others who may be able to provide pertinent information.

c. Use the following guidelines in completing the CDS-1 form:

Accurately record the demographic information, collecting as much information as possible, including name, age, address, telephone number, day care or preschool information and immunization status of the patient.

1) If the patient is hospitalized, collect hospital and transfer hospital information if applicable. Hospital laboratories and infection control professionals are key in obtaining the appropriate information for confirming a diagnosis.
2) Collect clinical information on the case including date of symptom onset, symptoms, laboratory data, treatment information, and outcome of disease (*e.g*., recovered, died). This information is best collected from the infection control professional at the hospital or the patient's healthcare provider.
3) Identify the household and day care contacts. Those who meet the definition of a close contact (see Section 4B below) of a case of invasive *H. influenzae* disease must be referred to their healthcare provider for appropriate antibiotic therapy.

NOTE: If CDRS is used to report enter collected information regarding exposure history, travel and any additional information into "Comments" section.

After completing the form, attach all lab report(s) and fax to the NJDHSS Infectious and Zoonotic Diseases Program. (The confidential fax number is 609.631-4863), or the report can be filed electronically over the Internet using the confidential and secure Communicable Diseases Reporting System (CDRS). Call the IZDP at 609.588.7500 to confirm receipt of the fax.

d. Institution of disease control measures is an integral part of case investigation. It is the health officer's responsibility to understand, and, if necessary, institute the control guidelines listed below in Section 4 "Controlling Further Spread."

4) CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements (N.J.A.C. 8:57-1.10)

Minimum Period of Isolation of Patient

Isolate the case until 24 hours after initiating appropriate antimicrobial treatment to eliminate carriage (currently only cefotaxime, ceftriaxone, and rifampin are known to eliminate carriage).

Minimum Period of Quarantine of Contacts

Where it has been determined that antimicrobial prophylaxis is necessary, children and staff should be excluded from the setting until rifampin has been started.

B. Protection of Contacts of a Case

1. **Isolate the case** until 24 hours after initiating appropriate antimicrobial treatment that eliminates carriage. Currently, only the treatment drugs cefotaxime and ceftriaxone are known to eradicate Hib from the nasopharynx. So, if the patient is treated with ampicillin or chloramphenicol instead, s/he must receive rifampin prophylaxis. Also, note that Hib disease does not necessarily confer immunity to subsequent disease. Immunize as follows:
   - **Children with invasive Hib disease at < 24 months of age—**immunize according to the age-appropriate schedule for unvaccinated children and as if they had received no prior doses. Begin 1 month after onset of disease or as soon as possible thereafter. For additional information, please refer to the table in Section 4 B. 3.
   - **Children with invasive Hib disease at ≥ 24 months of age—**no immunization is necessary, regardless of previous immunization status, because the disease probably induced a protective immune response and second episodes at this age are rare.

2. **Antimicrobial prophylaxis for close contacts.** Although several antibiotics are useful for *treatment* of invasive Hib disease and elimination of carriage in the case, rifampin is the appropriate drug to use for antibiotic *prophylaxis* of contacts. Several studies have shown that rifampin eradicated Hib carriage in ≥ 95% of contacts of primary Hib cases, including children in daycare facilities.

   When indicated, prophylaxis should be initiated as soon as possible. Most secondary cases in households occur in the first week after hospitalization of the index case. Prophylaxis of household contacts that begins ≥ 1 week after hospitalization of the case may still be of benefit, although initiation of prophylaxis beyond 4 weeks after that date is probably of limited utility. Prophylaxis is not recommended for pregnant women who are contacts because the effect of rifampin on the fetus has not been established.

Rifampin Prophylaxis against Hib	
Age Group	**Dosage/Schedule**
Infants < 1 month of age	10 mg/kg PO QD x 4 days
Children	20 mg/kg PO QD x 4 days (maximum: 600 mg/dose)
Adults	600 mg PO QD x 4 days

The risk of secondary disease in children attending child care centers appears to be lower than that observed for age-susceptible household contacts, and secondary disease in child care contacts is rare when all contacts are older than 2 years. Also, the efficacy of rifampin in preventing disease in child care groups is not established. Nevertheless, rifampin prophylaxis is recommended in certain situations, as indicated in the table below.

Indications and Guidelines for Rifampin in Chemoprophylaxis for contacts of Index Cases of Invasive *Haemophilus influenzae* Type b (Hib) Disease

Chemoprophylaxis recommended

- In certain index cases:
  - Index case, if treated with regimens other than cefotaxime or ceftriaxone. Chemoprophylaxis usually is provided just before discharge.
- In certain household situations:
  - All household contacts (except pregnant women),[1] irrespective of age, in households where at least 1 contact is < 48 months of age *and* is unimmunized or incompletely immunized.[1.]
  - All household contacts (except pregnant women),[1] irrespective of age, in households where a child is < 12 months of age, even if the primary series has been given.
  - All household contacts (except pregnant women),[1] irrespective of age, in households with an immunocompromised child, irrespective of the child's Hib immunization status.
- In certain child care situations:
  - Nursery and child care centers contacts where ≥ 2 cases occurred within 60 days, with ≥ 1 unimmunized or under immunized child < 48 months of age.[2,3]

Chemoprophylaxis *not* recommended

- In certain individuals:

- Pregnant women
- In certain household situations:
  - Occupants of households with no children < 48 months of age other than the index case.
  - Occupants of households when all household contacts < 48 months of age have completed their Hib immunization series.[4]
- In certain child care situations:
  - Nursery and child care contacts of 1 index case, when all contacts are > 24 months of age.
  - Nursery and child care contacts of 1 index case, when all children < 48 months of age have completed their Hib immunization series.[4]
  - Nursery and child care center contacts where ≥ 2 cases occurred within 60 days, when all children < 48 months of age have completed their Hib immunization series.[4]

[1] Defined as persons residing with the index patient or nonresidents who spent ≥ 4 hours with the index case for ≥ 5 of the 7 days proceeding the day of hospital admission of the index case.
[2] Only children who are age-appropriately immunized and on rifampin should be permitted to enter the child care center or setting during the time prophylaxis is given Children enrolling in the day care center or other setting during the time prophylaxis is given should also receive rifampin, as should supervisory personnel.
[3] When a single case has occurred, the advisability of rifampin prophylaxis in exposed child care setting with unimmunized or under immunized children is controversial, but many experts recommend no prophylaxis.
[4] Complete immunization is defined as having had ≥ 1 dose of conjugate vaccine at ≥ 15 months of age; 2 doses between 12 and 14 months of age; or a 2- or 3-dose primary series (number of doses required depends on vaccine type and age at initiation) when < 12 months with a booster dose at ≥ 12 months of age. Note that all infants (< 12 months of age) are by definition incompletely immunized.

3. **Ensure appropriate immunization of contacts.** The number of doses required is determined by the current age of the child and the number, timing, and type of Hib vaccine doses previously received. Unvaccinated and under vaccinated children < 5 years of age should be scheduled for completion of the recommended age-specific immunization schedule (see definition of "complete immunization" in Footnote 1 of the table above). Infants should be placed on an accelerated schedule using minimum intervals between doses. Unvaccinated high-risk individuals ≥ 5 years of age should receive one dose.

   The accelerated schedule for situations in which an incompletely vaccinated child has been exposed follows:

Accelerated schedule for Hib vaccination—to be used for unvaccinated and under vaccinated children (including all infants) after exposure to invasive Hib disease.

Type of Hib vaccine	Minimum age for first dose	Minimum interval from dose 1 to 2	Minimum interval from dose 2 to 3	Minimum interval from dose 3 to 4
HbOC (HIB-TITER®)	6 weeks	1 month	1 month	This booster at ≥ 12 mo. of age and ≥ 2 mo. after previous dose
PRP-T (ActHIB®, OmniHIB®)	6 weeks	1 month	1 month	
PRP-OMP (PedVax-HIB®)	6 weeks	1 month	This booster at ≥ 12 mo. of age and ≥ 2 mo. after previous dose	Not required

4. **Conduct surveillance.** Careful observation of exposed contacts, especially children < 4 years of age, is essential. Those in whom a febrile illness develops should receive prompt medical attention, regardless of Hib vaccination status.

D. Preventive Measures

Routine childhood vaccination is the best preventive measure against Hib disease. Good personal hygiene (which consists of proper hand-washing, disposal of used tissues, not sharing eating utensils, etc.) is also important.

Please consult the chapter on *Haemophilus influenzae* in the *Red Book* of the American Academy of Pediatrics for a full discussion of vaccines, immunization schedules, and special circumstances. For example, children, including those ≥ 5 years of age, with underlying conditions predisposing them to Hib disease may need additional doses.

ADDITIONAL INFORMATION

A *Haemophilus influenzae type b meningitis* Fact Sheet can be obtained at the NJDHSS website at <http://www.state.nj.us/health>.

The formal CDC surveillance case definition for invasive *H. influenzae* is the same as the criteria outlined in Section 2 A of this chapter. CDC case definitions are used by state health departments and CDC to maintain uniform standards for national reporting. For reporting to the NJDHSS, always refer to Section 2 A.

REFERENCES

American Academy of Pediatrics. Red Book 2000: Report of the Committee on Infectious Diseas. 25th Edition. Illinois, American Academy of Pediatrics, 2000.

CDC. Progress toward elimination of Haemophilus influenzae type b disease among infants and children—United States, 1987–1995. MMWR. 1996; 45:901–906.

CDC. Case Definitions for Infectious Conditions Under Public Health Surveillance. MMWR. 1997; 46:RR-10.

CDC. Manual for the Surveillance of Vaccine-Preventable Disease. CDC, 1999.

Chin J., ed. Control of Communicable Diseases Manual, 17th Edition. Washington, DC, American Public Health Association, 2000.

Massachusetts Department of Public Health, Division of Epidemiology and Immunization. Guide to Surveillance and Reporting. Massachusetts Department of Public Health, Division of Epidemiology and Immunization, January 2001

Schuchat A, et al. Active Bacterial Core Surveillance of the emerging infections program network. Emerg Infect Dis 2001; 7:92.